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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,514	02/16/2001	Jian-Bing Fan	A-68970-1/DJB/RMS/DCF	5362

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/785,514	FAN ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21-39* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18 and 21-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 15 September 2005 in which claims 14, 21, 23, 35-37 were amended and claims 19-20 were canceled. The amendments have been thoroughly reviewed and entered.

The amendments define the each population of microspheres as having a plurality of different analytes from an individula i.e. a first population of microsphers has a pluraltiy of analytes from a first individual and a second population of microspheres has a plurality of analytes from a second individual. Canceled, and previously examined, Claims 19-20 defined the microspheres as having a plurality of analytes from different "target source" i.e. patients.

The previous rejections in the Office Action dated 26 May 2005 are maintained. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection, based on the amendments using different terminology than previously examined and now canceled Claims 19-20, are discussed.

Claims 14-18, 21-39 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 14-18, 21-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Chee et al (U.S. Patent No. 6,355,431, filed 3 March 2000 and claiming priority to 20 May 1999).

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Regarding Claim 14, Chee et al disclose the method comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein the microspheres of each subpopulation comprises a plurality of different target analytes from a different individual (i.e. different samples) and covalently attached to the surface (e.g. following hybridization, crosslinking agents are added to cross-link the target "i.e. covalently attach" (Column 11, lines 1-5) wherein the microspheres are distributed on the surface (Column 38, lines 52-54). The method further comprising contacting the array with a first set of read out probes (e.g. amplifier probes, Column 34, line 32-Column 36, line 14) to detect the presence of a first target analyte (Claim 1). Chee et al disclose the method wherein the target sequences are from individual i.e. patients (Column 56, lines 25-30).

Chee teaches the newly claimed microsphere subpopulations having multiple and different analytes in the discussion of their arrays, composite arrays and array of arrays (e.g.Col 38-44)i.e. an "array of arrays" allows simultaneous analysis of multiple samples (Column 38, lines 5-14) wherein the "composite arrays" comprise individula and different arrays for assays on 96 different samples (Column 40, lines 36-42) and wherein "samples" are defined as e.g. mammalian, human (Column 7, lines 44-55). The array of Chee are

encompassed by the claimed "subpopulation". Because Chee teaches multiple arrays having different samples, Chee teaches the multiple subpopulations as claimed.

Regarding Claim 15, Chee et al disclose the method further comprising contacting the array composition with a second set of readout probes (Column 35, lines 23-57 and Column 36, lines 15-23).

Regarding Claim 16, Chee et al disclose the method wherein the microspheres are randomly distributed on the surface (Claim 30).

Regarding Claim 17, Chee et al disclose the method wherein the first set of readout probes comprises at least first and second probes wherein the first and second probes are differentially labeled (Column 35, lines 42-57).

Regarding Claim 18, Chee et al disclose the method further comprising detecting the firs label as an indication of the first target analyte (Column 35, lines 42-57).

Regarding Claim 19, Chee et al disclose the method wherein the first and second subpopulations comprise analytes from first and second sources e.g. multiplex detection of different polymorphisms (Column 56, line 63-Column 57, line 19).

Regarding Claim 20, Chee et al disclose the method wherein the different sources are patients (Column 56, lines 23-32).

Regarding Claim 21, Chee et al disclose the method of genotyping comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. capture probe and modified primer) wherein a plurality of different targets are covalently attached to the surface (i.e. target-probe ligation product to microspheres comprising individual probes (Column 43, lines 36-37) or universal probes whereby differing targets ligate to from different analytes (Column 34, lines 35-55) and (Column 9, lines 21-24, and Fig. 7) wherein the microspheres are randomly distributed on the surface. The method further comprising contacting the array with a first set of extension

probes that hybridize adjacent to a detection position, contacting with a nucleotide and an polymerase to extend the extension probe and detecting the presence of the nucleotide (Fig. 2A/2B and Claim 5).

Regarding Claim 22, Chee et al disclose the method wherein the nucleotide comprises a label (Fig. 2A/2B and Column 6, lines 9-16).

Regarding Claim 23, Chee et al disclose the method of determining the identification of a nucleotide comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes (i.e. capture probe and modified primer) wherein a plurality of different targets are covalently attached to the surface (i.e. target-probe ligation product to microspheres comprising individual probes (Column 43, lines 36-37) or universal probes whereby differing targets ligate to from different analytes (Column 34, lines 35-55) and (Column 9, lines 21-24, and Fig. 7) wherein the microspheres are randomly distributed on the surface. The method further comprising forming hybridization complex between the target sequence and a readout probe and determining the nucleotide at the detection position label (Fig. 2A/2B; Column 6, lines 9-16; and Claim 5).

Regarding Claim 24, Chee et al disclose the method wherein the target comprises a first and second target domain and the hybridization complex comprises a first readout probe hybridized to the first domain and a second readout probe hybridized to the second domain and said determining comprising adding a ligase (Column 17, line 55-Column 18, line 67 and Claim 6).

Regarding Claim 25, Chee et al disclose the method wherein the first readout probe comprises a label (Column 17, line 55-Column 18, line 67).

Regarding Claim 26, Chee et al disclose the method further comprising contacting the hybridization complex with at least a first nucleotide and a polymerase to extend the first

readout probe wherein the nucleotide is complementary to the detection position (Column 18, lines 9-18).

Regarding Claim 27, Chee et al disclose the method wherein the substrate is a fiber optic bundle (Claim 28).

Regarding Claim 28, Chee et al disclose the method wherein the substrate is glass or plastic (Claim 29).

Regarding Claim 29, Chee et al disclose the method further comprising contacting the microspheres with decoder binding ligands and the microspheres comprise identifier binding ligand (Column 49, lines 16-20).

Regarding Claim 30, Chee et al disclose the method wherein the target comprises target sequences (Column 9, lines 14-25).

Regarding Claim 31, Chee et al disclose the method wherein the target sequences comprises target nucleic acids (Column 9, lines 14-25).

Regarding Claim 32, Chee et al disclose the method wherein the target comprises target genomic DNA sequences (Column 9, lines 14-25).

Regarding Claim 33, Chee et al disclose the method wherein the target sequences comprises target nucleic acids (Column 9, lines 14-25).

Regarding Claim 34, Chee et al disclose the method wherein the target nucleic acids comprises target genomic DNA (Column 9, lines 14-25).

Regarding Claim 35, Chee et al disclose the method comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes attached to the microspheres via receptor-ligand interaction and wherein the analytes are derivatized with a receptor or ligand (e.g. restriction site Column 21, lines 1-14) wherein the microspheres are distributed on the surface (Column 38, lines 52-54). The method further comprising contacting the array with a first set of read out probes (e.g.

amplifier probes, Column 34, line 32-Column 36, line 14) to detect the presence of a first target analyte (Claim 1).

Regarding Claim 36, Chee et al disclose the method of genotyping comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes attached to the microspheres via receptor-ligand interaction and wherein the analytes are derivatized with a receptor or ligand (e.g. restriction site Column 21, lines 1-14) wherein the microspheres are randomly distributed on the surface. The method further comprising contacting the array with a first set of extension probes that hybridize adjacent to a detection position, contacting with a nucleotide and an polymerase to extend the extension probe and detecting the presence of the nucleotide (Fig. 2A/2B and Claim 5).

Regarding Claim 37, Chee et al disclose the method of determining the identification of a nucleotide comprising providing an array composition comprising a substrate having discrete sites and a population of microspheres containing first and second subpopulations wherein each microsphere comprises a plurality of different target analytes attached to the microspheres via receptor-ligand interaction and wherein the analytes are derivatized with a receptor or ligand (e.g. restriction site Column 21, lines 1-14) wherein the microspheres are randomly distributed on the surface. The method further comprising forming hybridization complex between the target sequence and a readout probe and determining the nucleotide at the detection position label (Fig. 2A/2B; Column 6, lines 9-16; and Claim 5).

Regarding Claims 38 and 39 Chee et al further teach the embodiment wherein the microspheres are coated with streptavidin and the ligand is biotin (Column 33, lines 33-45).

Response to Arguments

4. Applicant traverses the finality of the previous office action. The finality is withdrawn. This action is made final.

Chee teaches the newly claimed microsphere subpopulations having multiple and different analytes in the discussion of their arrays, composite arrays and array of arrays (e.g.Col 38-44)i.e. an "array of arrays" allows simultaneous analysis of multiple samples (Column 38, lines 5-14) wherein the "composite arrays" comprise individula and different arrays for assays on 96 different samples (Column 40, lines 36-42) and wherein "samples" are defined as e.g. mammalian, human (Column 7, lines 44-55). The array of Chee are encompassed by the claimed "subpopulation". Because Chee teaches multiple arrays having different samples, Chee teaches the multiple subpopulations as claimed.

Applicant asserts that Chee does not teach a plurality of different targets attached to a microsphere. The argument has been considered but is not found persuasive because, as cited above, Chee provides three embodiments meeting the limitations of the claims. Furthermore, the instant specification defines the claimed "target analyte" as provided below (page 6, last paragraph):

> The present invention is directed to the detection of patient sample components or target analytes. By patient sample components" or "target analytes" or grammatical equivalents herein is meant any molecule in the sample, which is to be detected, with proteins and nucleic acids being preferred, and nucleic acids being particularly preferred.

First, Chee teaches a target comprising two target domains (analytes) attached to the microsphere (Column 18, lines 3-18 and lines 61-62). Second, Chee et al teach target-probe ligation product immobilized on microspheres comprising individual probes (Column 43, lines 36-37) wherein the microspheres further comprise identifier binding ligands (IBL) that are target analytes for specifically binding decoder binding ligands (Column 44, lines 8-27) wherein the IBLs are naturally occurring (Column 44, lines 34-37). Finally, Chee et al teach the method wherein each microspheres comprises a plurality of different IBLs (Column 45, lines

65-Column 46, line 13) each of which is an analyte for a DBL (Column 46, lines 33-39) wherein the IBLs are naturally occurring (Column 44, lines 34-37). Therefore, Chee teaches the plurality of target analytes as claimed.

Applicant asserts that the instant specification defines target analyte over that taught by Chee. Applicant underlines, the term "molecule" and appears to be asserting that this definition of target requires that the entire target (i.e. entire molecule) is detected thereby differing from Chee's multiple target domains within a target. The assertion is noted, however, neither the claims nor specification define the target detection or its detection as an entire molecule. Furthermore, it is unclear what would be required to detect an entire molecule i.e. would a nucleic acid probe have to fully complementary in length and sequence to detect an entire target?

Applicant asserts (page 12, last paragraph) that Chee does not teach a plurality of different target analytes covalently attached to a microsphere. The assertion is noted, however, the instant claims, as amended, do not require different analytes on a microsphere. In contrast, the claims define a subpopulation of microspheres having different analytes i.e. multiple microspheres and multiple analytes. However, if the claims would require multiple analytes/microsphere the multiple target domains (and etc) discussed in the previous office action are encompassed by the multiple targets. Chee specifically defines the target domains as "target" domains (Column 9, lines 40-59). Furthermore, the methods of Claims 34-39 merely require target attachment via receptor-ligand interaction and do not require covalent attachment.

The claims, as amended, are interpreted to require each subpopulation of microspheres to have multiple and different analytes. However, even if, as asserted, the claims require multiple targets per microsphere, Chee et al teaches three different embodiments that meet this limitation. The following citations are reiterated from the previous office action.

First, Chee et al teach the target a target nucleic acid comprises two "target domains" and is immobilized on the microsphere (Column 18, lines 3-18 and lines 61-62). Given the

broadest reasonable interpretation, the claimed "target analyte" encompasses the "target domains" taught by the reference because each domain functions as an analyte for domain-specific primer binding.

Second, Chee et al teach target-probe ligation product immobilized on microspheres comprising individual probes (Column 43, lines 36-37) wherein the microspheres further comprise identifier binding ligands (IBL) that are target analytes for specifically binding decoder binding ligands (Column 44, lines 8-27).

Finally, Chee et al teach the method wherein each microspheres comprises a plurality of different IBLs (Column 45, lines 65-Column 46, line 13) each of which is an analyte for a DBL (Column 46, lines 33-39).

Any one of the three embodiments illustrate different analytes attached to each microsphere. However, the claims are not so limited.

The claims are interpreted as being drawn to multiple microsphere subpopulations, each having multiple analytes attached. Many of the arguments address multiple analytes per microsphere. These arguments are not commensurate in scope with the claims.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Primary Examiner
Art Unit: 1634
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